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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/829,201	04/22/2004	Daniel J. Drucker	50821/78.4	5544

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STOEL RIVES LLP - SLC
201 SOUTH MAIN STREET, SUITE 1100
ONE UTAH CENTER
SALT LAKE CTY, UT 84111

EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/829,201	DRUCKER ET AL.	
	Examiner	Art Unit	
	DONG JIANG	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 6-13* is/are pending in the application.

4a) Of the above claim(s) *7-11* is/are withdrawn from consideration.

5)☒ Claim(s) *1* is/are allowed.

6)☒ Claim(s) *12 and 13* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☒ Claim(s) *1 and 6-13* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/10/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's amendment filed on 14 April 2010 is acknowledged and entered. Following the amendment, claims 1 and 6 are amended, and the new claims 12 and 13 are added.

Currently, claims 1 and 6-13 are pending, and claims 1, 6, 12 and 13 are under consideration. Claims 7-11 remain withdrawn from further consideration as being drawn to a non-elected invention.

Withdrawal of Objections and Rejections:

The rejection of claims 1 and 6 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of applicant's amendment.

The prior art rejection of claims 1 and 6 under 35 U.S.C. 103(a) as being unpatentable over Christensen et al. (Nature Med., July 2000, 6(7): 802-807), and in view of Drucker et al. (US5,789,379, 8/4/98) is withdrawn in view of applicant's amendment.

Formal Matters:

Claims

Claim 6 is objected to for the following informalities, and appropriate correction is required for each item:

The claim recites "a pharmaceutical composition as defined in claim 1". The following is suggested: "*the* pharmaceutical composition as defined in claim 1".

Rejections under 35 U.S.C. §112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 is indefinite for the recitation "are formulated separately, but *associated physically*" because it is unclear what it is meant, for example, whether it means the two formulations are mixed together ("associated physically"), or something else. The specification states "[T]he term "pharmaceutical combination" embraces physical combinations of the inhibitor and the enhancer; it is to be appreciated, however, that other forms of such combinations are also suitable and are embraced by the term. In one embodiment, for instance, the inhibitor and the enhancer are formulated together; in other embodiments the inhibitor and the enhancer are *formulated separately*, but *associated physically for instance in kit form* containing the separate formulations and instructions for their use in combination to treat a target medical condition" (page 11, [0029]). "Associated physically" usually means the two things are attached or linked together. However, since the specification "defines" "associated physically" in a special example, the following is suggested "are formulated separately, but associated physically in kit form containing the separate formulations" if that is intended.

Claim 13 is included in this rejection because it is dependent from the specifically mentioned claims without resolving the indefiniteness issue belonging thereto.

Rejections Over Prior Art:

Claim interpretation: As the claims are indefinite for the reasons above, claim 12 is *interpreted* as drawn to a combination comprising Gly2GLP-2 and exendin (9-39), wherein said Gly2GLP-2 and exendin (9-39) are formulated separately, and contained in a kit as the separate formulations.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tang-Christensen et al. (Nature Med., July 2000, 6(7): 802-807, provided by applicants), and in view of Drucker et al. (US5,789,379, 8/4/98), for the same reasons in the rejection of claims 1 and 6 under 35 U.S.C. 103(a) as being unpatentable over the same references set forth in the last Office Action mailed on 10/14/09, at pages 3-4.

Tang-Christensen reported a study investigating the role of GLP-2 and GLP-1 in food intake, wherein rats were centrally administered (intracerebroventricaular injection, icv) GLP-2, exendin(9-39) (a GLP-1 antagonist), or both (page 803, 2nd column, and Figure 3c, for example).

Tang-Christensen does not teach the use of Gly_2GLP-2 in combination with exendin(9-39) in the study. However, Gly_2GLP-2, like exendin(9-39), is well known in the art as a GLP-2 analog.

Drucker teaches GLP-2 analogs, which posses advantageous properties. Drucker teaches, for example, that replacing the Ala at position 2 of the GLP-2 peptide with an alternative amino acid such as Gly_2 would confer the peptide resistance to cleavage by human DPP-IV enzyme while retaining the GLP-2 activity (column 2, lines 32-33 and 56-59; claim 19, line 4; and column 15, Table 1, #4 and 6).

Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to use a GLP-1 analog such as Gly_2GLP-2 (taught by Drucker) in combination with exendin(9-39) for studying the role of GLP-2 and GLP-1 in food intake in the experiments taught by Tang-Christensen, since Gly_2GLP-2 is a functional analog of GLP-2 (therefore, they are interchangeable). Note, the present claims do not require that the claimed pharmaceutical combination to be a mix (or a composition) of Gly_2GLP-2 and exendin(9-39). Thus, Tang-Christensen's use of the two agents together would qualify them as "a pharmaceutical combination". The person of ordinary skill in the art would have been motivated

to use Gly_2GLP-2 and exendin(9-39) together for studying food intake, and potential therapeutics related to food intake, and reasonably would have expected success because Drucker has demonstrated that Gly_2GLP-2 is a GLP-2 analog possessing the functional property of GLP-2. With respect to the kit in claim 6, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to make a kit containing said agents, because such a kit would facilitate its commercial distribution for uses such as research indicated by Tang-Christensen. Further, packing two well known agents in a kit would not be considered to constitute a novel inventive concept.

Applicants argument filed on 14 April 2010 has been fully considered, but is not deemed persuasive for the reasons below.

At pages 5-6 of the response, the applicant argues that there was no reasonable expectation of success because Tang-Christensen teaches: 1) co-administration of GLP-2 and Exendin (9-39) has no effect compared to the control in appetite suppression; and 2) Exendin (9-39) does not enhance GLP-2 mediated anorexia, it reverses it, thus, a person of ordinary skill in the art could not have reasonable expectation of success in combining GLP-2 or GLP-2 analogs (in view of Drucker) with Exendin (9-39) to enhance the anorectic effects of said GLP-2 or GLP-2 analog, because the prior art clearly taught that the opposite was true. This argument is not persuasive because the issue is not whether there was a reasonable expectation of success regarding appetite suppression from the teachings of the prior art reference, rather, issue is whether there was a reason to put the two well known compositions together, for example, in a kit; and whether a person having ordinary skill in the art would be able to put the two separate formulations together successfully as the claims are directed to a combination comprising two separate formulations. As addressed above, Tang-Christensen teaches a method of studying the effect of GLP-2 and GLP-1 on food intake in an animal model using GLP-2 and exendin(9-39) (a GLP-1 antagonist), indicating GLP-2 and exendin(9-39)/GLP-1 are involved in regulating food intake. Therefore, it would be obvious to put the two separate compositions together, for example, in a kit, to facilitate research and drug development in the field of regulating food intake. Further, it is certain that a person having ordinary skill in the art would be able to put the

two separate formulations together successfully in a kit as packing pharmaceutical compositions/reagents in a kit is old and well known in the art.

At page 6 of the response, the applicant argues that the prior art references were improperly combined, that the references cited by the Examiner cannot be combined to establish the obviousness of the claimed enhancement of Gly2GLP-2's anorectic effects by Exendin (9-39) where one of the references (Tang-Christensen) specifically teaches that Exendin (9-39) reverses the anorectic effects of GLP-2, and that where Tang-Christensen teaches that GLP-2 and Exendin (9-39) combined have no appetite suppressing effects, the references cannot be combined to make obvious an invention that explicitly claims an anorectic effect. This argument is not persuasive for the reasons above. Once again, the question at issue is not about what effect it may be when said two separate compositions used together, rather, the question is whether there was a reason to put the two separate compositions together, for example, in a kit. To achieve appetite suppressing effects is not the only reason to put the two separate compositions together in a kit.

At pages 6-7 of the response, the applicant argues that Tang-Christensen specifically teaches that Exendin (9-39) reverses the anorectic effects of GLP-2, however, the present specification teaches that "[r]emarkably, the inhibitory effects of icv hGly2GLP-2 on food intake in wild type mice were significantly more pronounced in the presence of co-administered exendin (9-39)", which contradict the knowledge available to a person of ordinary skill in the art and represent an unexpected result over the prior art. This argument is not persuasive for the reasons addressed above.

Conclusion:

Claim 1 is allowed.

Claim 6 would be allowable if amended to overcome the objection thereto.

Advisory Information:

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Dong Jiang/
Primary Examiner, Art Unit 1646
6/20/10